



# Quadrivalent Live Attenuated Influenza Vaccine (Q/LAIV)

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# Overview

- ◆ Transitioning from trivalent formulation of live attenuated influenza vaccine to a quadrivalent formulation
- ◆ Approved for use in the U.S on February 29<sup>th</sup>, 2012 under brand name FluMist® Quadrivalent (Influenza Vaccine Live, Intranasal)
  - Will be available in U.S. for 2013-2014 influenza season
- ◆ Addresses co-circulation of B strains from 2 lineages
- ◆ Quadrivalent formulation identical to trivalent formulation with exception of additional B strain
  - Same manufacturing process and excipients
  - Same intranasal delivery and dose volume (0.2 mL)
  - Same strain-specific potency of  $10^{7.0.5}$  FFU

# Switch to Quadrivalent Formulation Will Not Affect Reliable Supply and Early Availability of Q/LAIV

## ◆ Q/LAIV is not expected to impact:

- WHO/VRBPAC vaccine strain selection and reagent production
- MedImmune vaccine strain production capacity
  - More than 4 new LAIV strains are routinely and reliably produced every season using reverse genetics
- Bulk production
  - Improved bulk manufacturing capacity and cycle times will more than offset any additional demands of including four vaccine strains
- Will not delay availability of vaccine

# Q/LAIV Studies

- ◆ Two primary studies conducted:
  - Adult study (N = 1,800), initiated in 2009
  - Pediatric study (N = 2,312), initiated in 2010
  
- ◆ Additional study conducted - different delivery device
  - Adult study (N =1,800), initiated in 2009
  - Data used for safety analyses as Q/LAIV administered with new delivery system

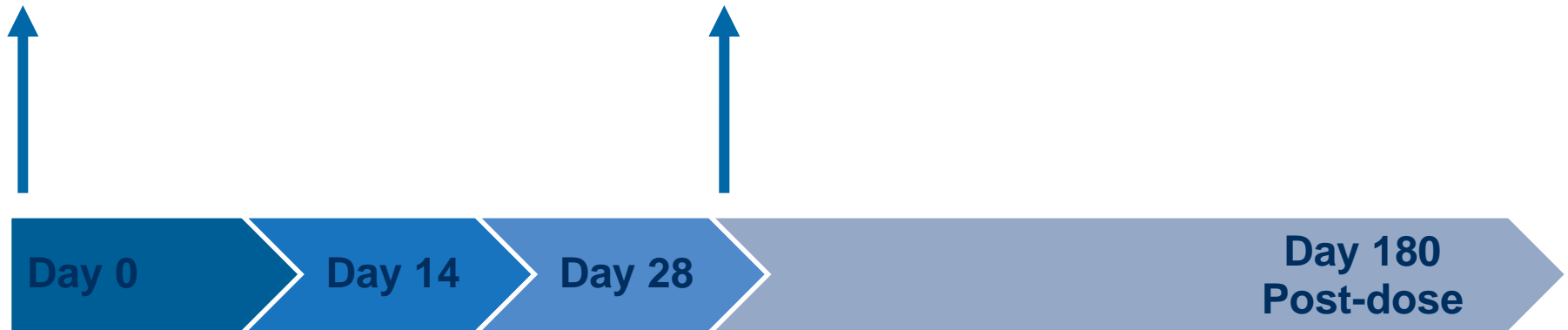
# Study Design: Adult Study and Pediatric Subjects 9 – 17 Years of Age (One Dose)

**Day 0**

**Randomization**

**Day 28**

**Immunogenicity  
Assessed**



← Solicited symptoms →

← Adverse events →

← Serious events and new onset chronic diseases →

# Study Design: Pediatric Subjects 2 – 8 Years of Age (Two Doses)

**Day 0**

**Randomization**

**Dose 1**

**Day 28**

**Immunogenicity  
Assessed**

**Dose 2**

**Day 28**

**Immunogenicity  
Assessed**



← Solicited symptoms →



← Adverse events →

← Serious events and new onset chronic diseases →

# Primary and Secondary Immunogenicity Endpoints Used in the Q/LAIV Studies

## ◆ Primary Endpoint

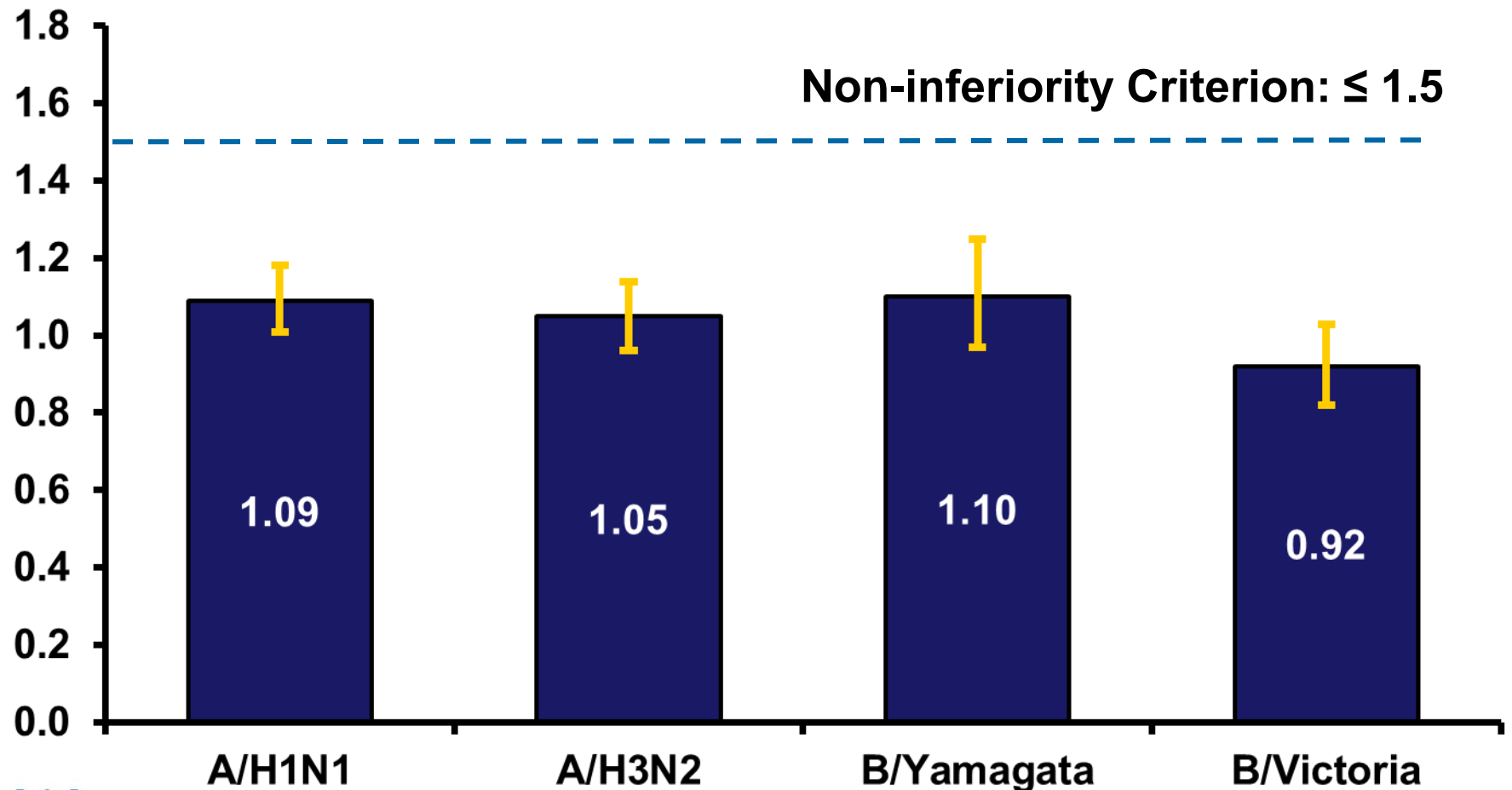
- Agreed upon with FDA
- Antibody titers measured after vaccination
- Ratio of titers calculated (T/LAIV / Q/LAIV)
- Ratio of 1 indicates identical immunogenicity
- Upper bound of 95% CI for ratio had to be  $\leq 1.5$  for all 4 strains

## ◆ Secondary Endpoints

- Seroconversion/seroresponse rates ( $\geq 4$ -fold rise in antibody titer)
- Proportion of subjects achieving antibody titers of  $\geq 32$

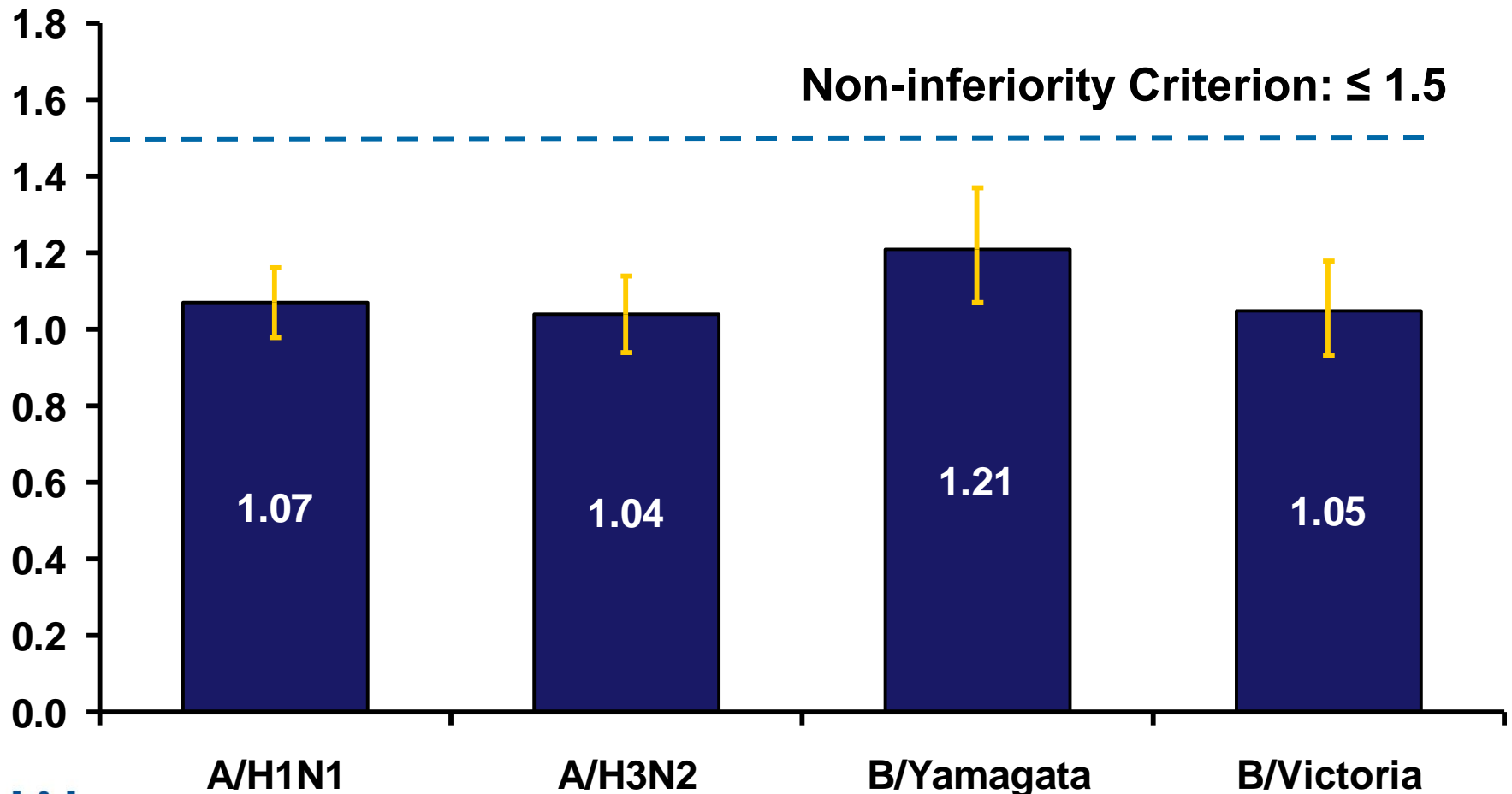
# Adult Study Met Primary Endpoint: Q/LAIV Non-inferior to T/LAIV

HAI GMT Ratio (T/LAIV / Q/LAIV)



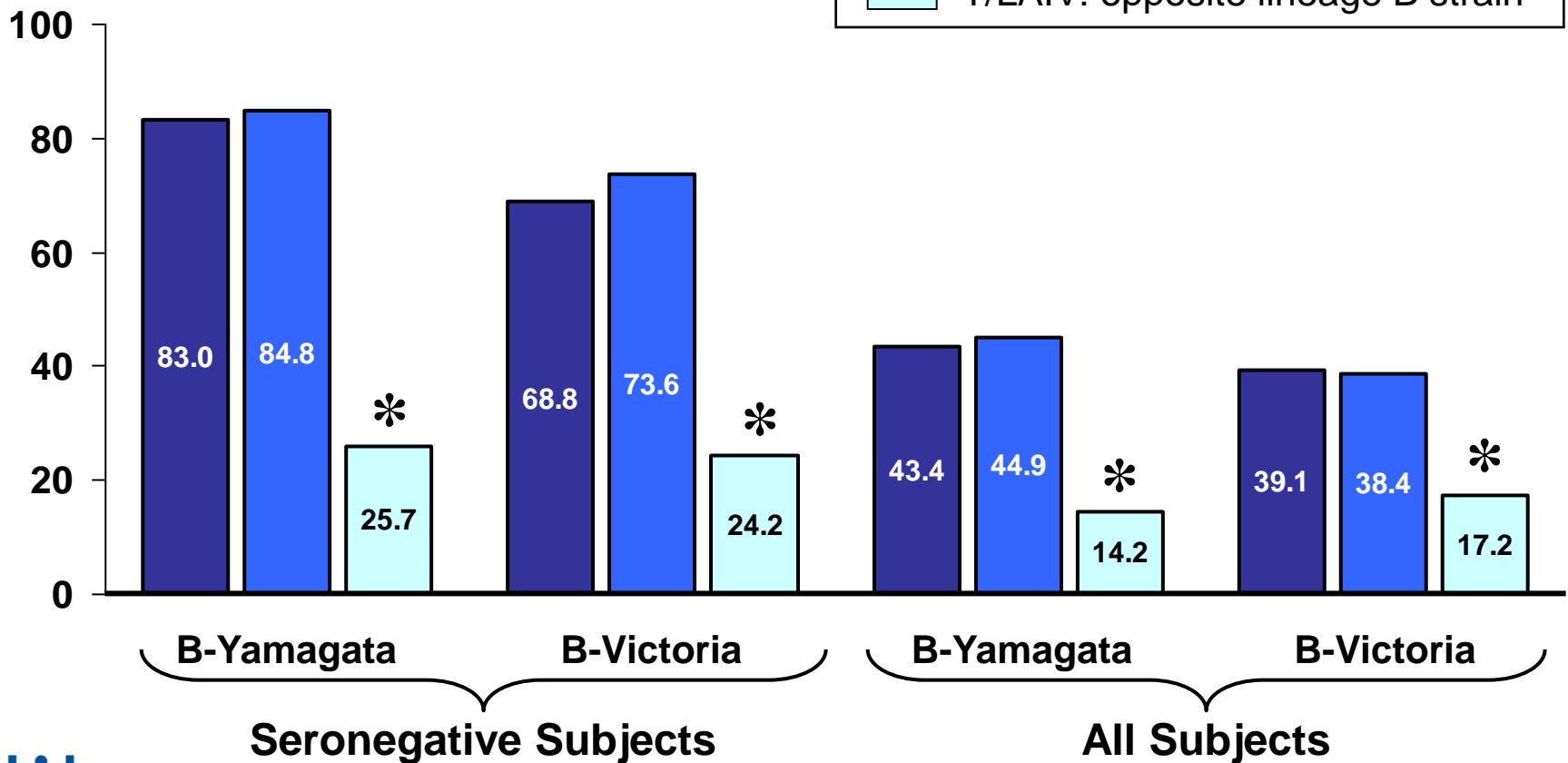
# Pediatric Study Met Primary Endpoint: Q/LAIV Non-inferior to T/LAIV

HAI GMT Ratio (T/LAIV/ Q/LAIV)



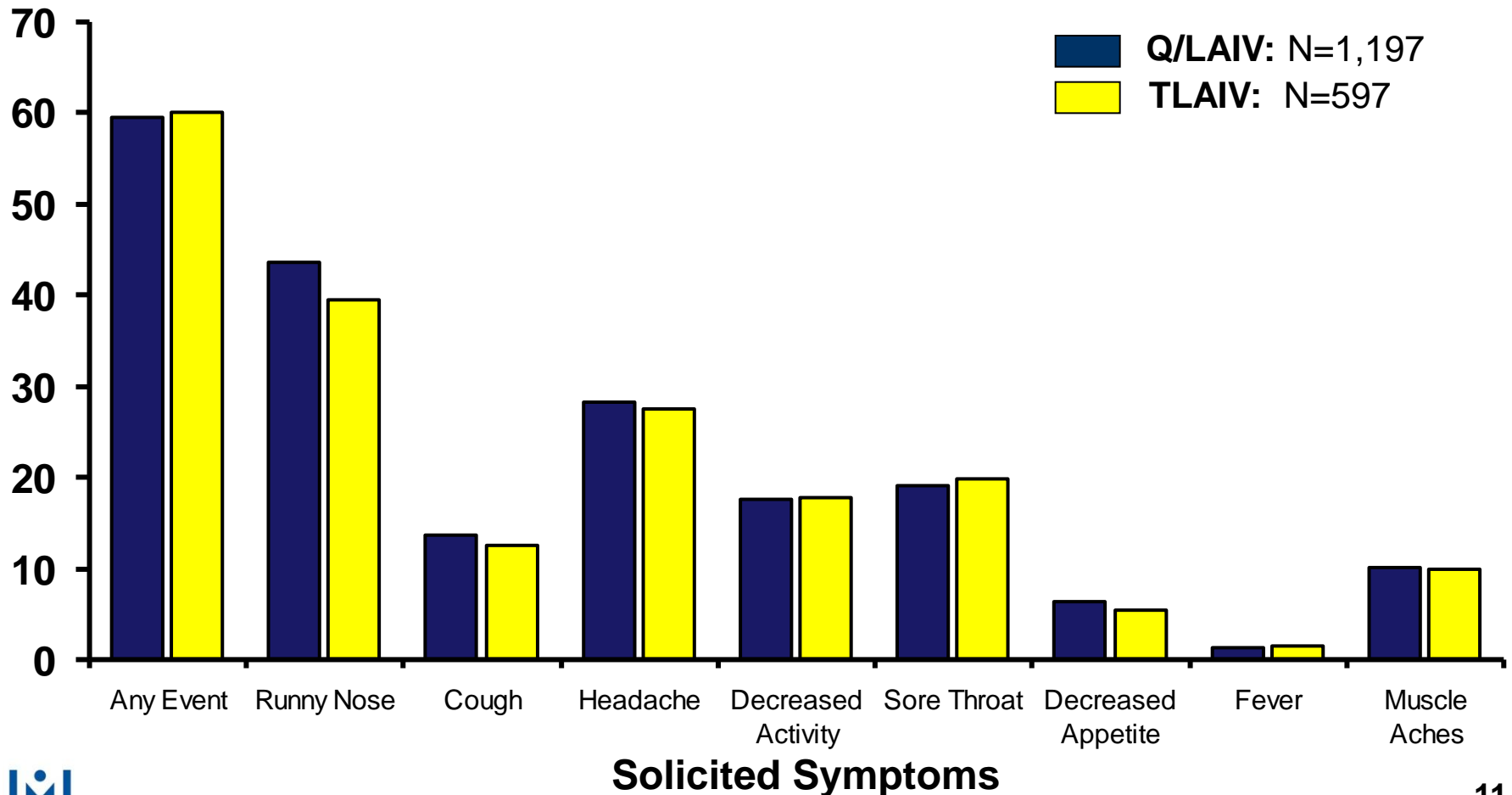
# Q/LAIV induced higher immune responses for B strains not contained in trivalent comparators

**Seroconversion/Seroresponse Rate  
(by baseline serostatus), %**



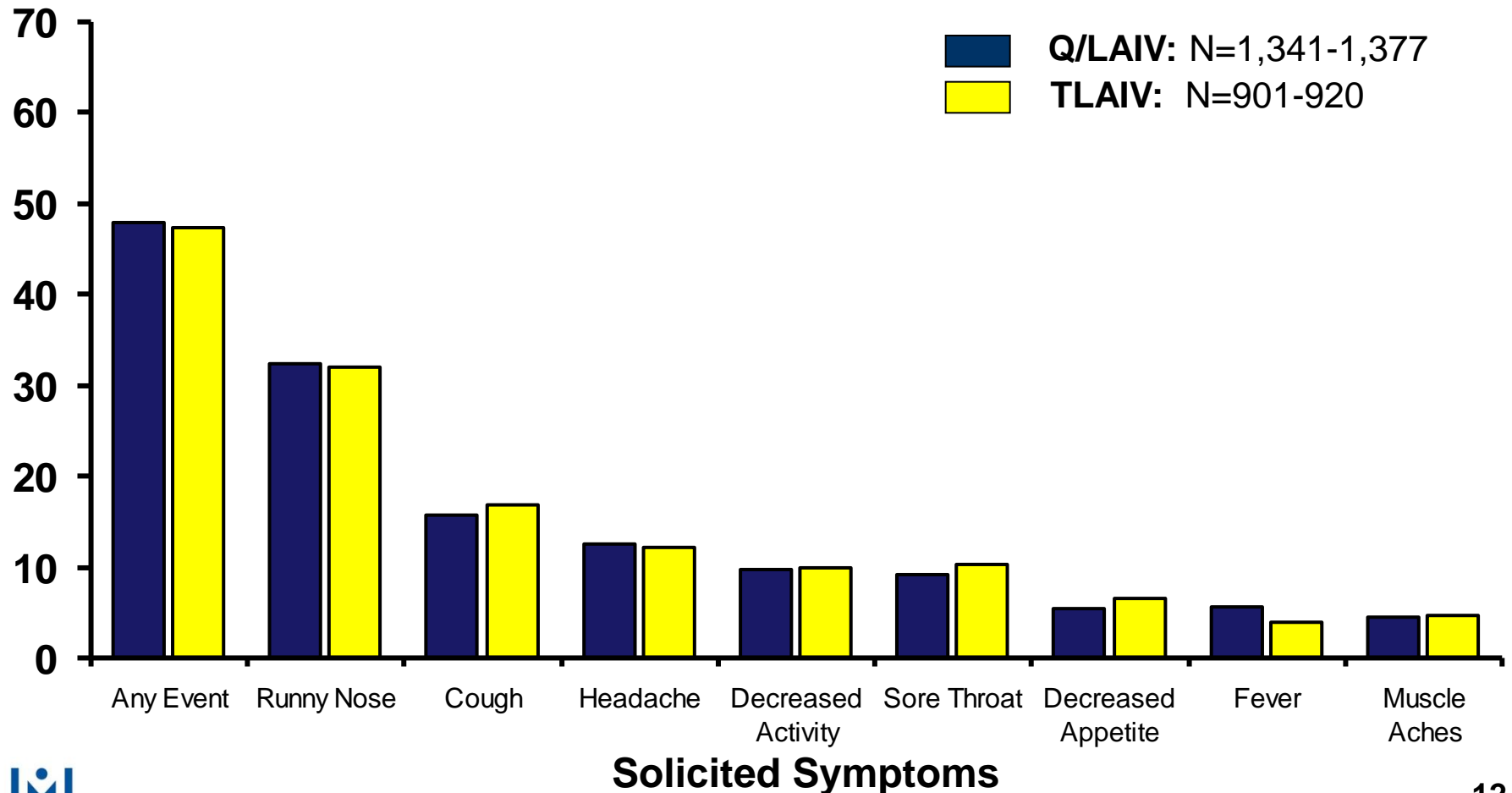
# Solicited Symptom Profile in Adults, Days 0-14

**Subjects with Solicited Symptoms Days 0-14 (%)**



# Solicited Symptom Profile in Children/Adolescents, Days 0-14

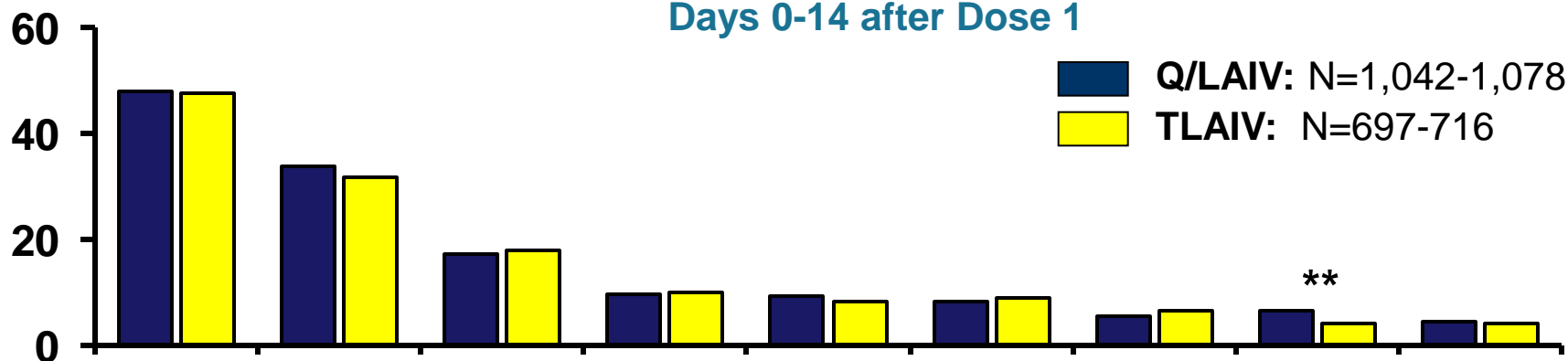
**Subjects with Solicited Symptoms Days 0-14 (%)**



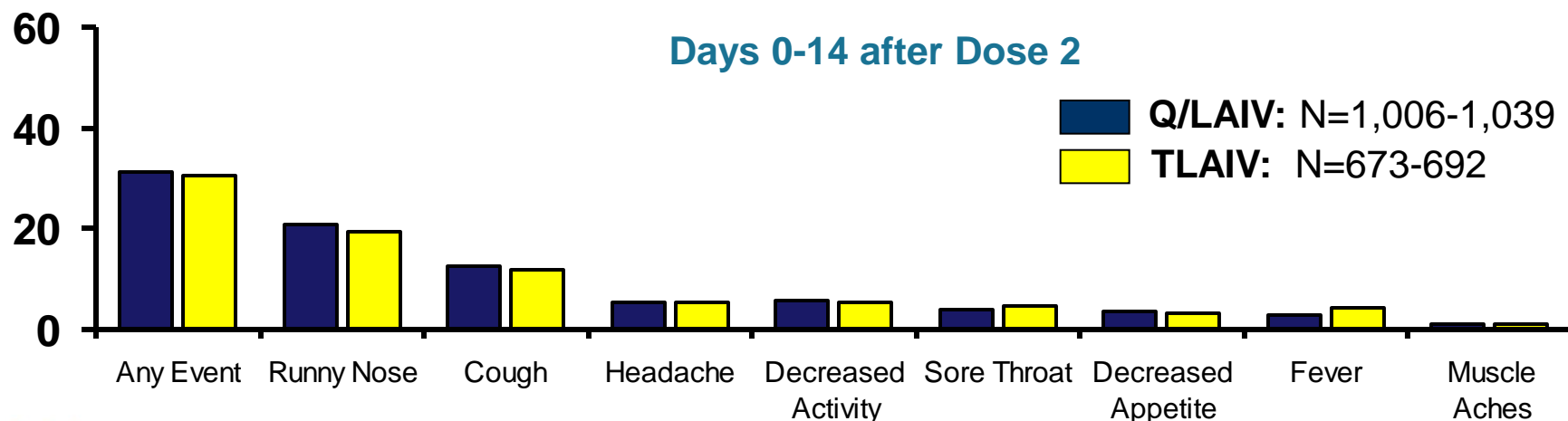
# Solicited Symptom Profile After Each of Two Doses in Children 2-8 Years of Age

## Subjects Experiencing Solicited Symptoms (%)

Days 0-14 after Dose 1



Days 0-14 after Dose 2



Solicited Symptoms

# Adverse Events

- ◆ Incidence of adverse event similar between Q/LAIV and T/LAIV
  - Adults\*: Q/LAIV 16.6%, T/LAIV 17.3%
  - Pediatric Study, Dose 1: Q/LAIV 21.0%, T/LAIV 20.7%
  - Pediatric Study, Dose 2: Q/LAIV 13.4%, T/LAIV 16.7%
- ◆ No evidence for wheezing signal
- ◆ 2 SAEs considered to be possibly/probably related to dosing
  - Spontaneous abortion (Q/LAIV, adult study with new delivery system) – possibly related
  - Hypersensitivity (T/LAIV, adult study) – probably related
- ◆ No related new onset chronic diseases
- ◆ No deaths in Q/LAIV pivotal adult or pediatric studies



# Overall Summary

- ◆ Transitioning T/LAIV to quadrivalent formulation
- ◆ Q/LAIV immunogenicity non-inferior to T/LAIV
  - Studies met primary non-inferiority endpoints
  - Secondary endpoints consistent with primary endpoint
- ◆ Q/LAIV demonstrated higher immune responses to B strains not contained in T/LAIV comparators
- ◆ Q/LAIV has a favorable safety profile, comparable to the trivalent formulation
- ◆ QLAIV expected to have efficacy/effectiveness profile similar to that of T/LAIV but with broader coverage of B strains